IMPLEMENTING REGULATORY POLICIES TO UNLOCK THE POTENTIAL OF GENE EDITING IN AGRICULTURE: BUILDING ON THE SUCCESSES OF THE UNITED STATES COORDINATED FRAMEWORK FOR THE REGULATION OF BIOTECHNOLOGY

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I. INTRODUCTION

Our food system[1] can be better. This is not an indictment, but rather a recognition of the incredible potential recent agricultural innovations can provide to enhance our efforts of sustainably producing healthy and nutritious food into the future. Increasing agricultural sustainability and reliance are even more imperative when you consider that according to the United Nations Food and Agriculture Organization, the worldwide number of undernourished people—after a period of decrease—has been increasing since 2014 and reached an estimated 820 million people in 2018.[2] With this considered, increasing agricultural sustainability and resilience is imperative.

One innovation in particular that has the potential to significantly assist in addressing these challenges is gene editing. Gene editing is a set of tools, including the well-known CRISPR-Cas9, that can be used to precisely and efficiently modify the genome of agricultural crops.[3] Modifications could be

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1. *The future food system: the world on one plate?*, COMM. WORLD FOOD SEC. (Oct. 20, 2016), https://perma.cc/GLA9-LBYY ("a food system encompasses all the stages of keeping us fed: growing, harvesting, packing, processing, transforming, marketing, consuming and disposing of food.").

2. FOOD AND AGRIC. ORG. OF THE UNITED NATIONS ET AL., THE STATE OF FOOD SECURITY AND NUTRITION IN THE WORLD 3 (2019), https://perma.cc/395R-5Z7E.

3. NAT'L ACAD. OF SCI. Eng'g Med., GENETICALLY ENGINEERED CROPS: EXPERIENCES

aimed at creating plants better adapted to changing climates, have a reduced environmental impact, are resistant to disease, and even have improved nutritional value.[4] To realize these potential benefits and many more, however, our regulatory policies must promote and enable access to these innovative plant products. Regulatory policies must likewise continue to protect human health and the environment, which can be done without implementing overly precautious policies that risk stifling adopting of innovation that can positively impact our food system's ability to sustainably adapt into the future.

II. REGULATORY PRINCIPLES TO ENABLE AGRICULTURAL INNOVATION

Multiple Presidential Administrations through Executive Orders and agency policy statements have outlined regulatory principles to serve as guideposts in policy formation "to achieve regulatory goals that are designed to promote innovation."[5] The principles include making decisions based on the best available scientific and technical information, being efficient while commensurate with risk, accommodating new evidence and learning, and being consistently applied and enforced.[6] These foundational tenets are relevant across industry sectors and products, and have meaningful importance as regulatory frameworks for implementing innovative new products. During the Clinton Administration, the White House Office of Management and Budget stated, "[e]xcessive or poorly designed regulations . . . can cause confusion and delay, give rise to unreasonable compliance costs in the form of capital investments, labor and on-going paperwork, retard innovation, reduce productivity, and accidentally distort private incentives."[7]

Moreover, science-based and risk-proportionate regulation that adhere to these principles is important so the United States can lead efforts aimed at international regulatory harmonization of global frameworks to foster innovation. For example, the recent United States, Mexico, Canada Agreement (USMCA) sets forth a helpful standard for future international trade agreements.[8] The

AND PROSPECTS 23 (2016) [hereinafter GENETICALLY ENGINEERED CROPS].

4. *See id.* at 23-25.

5. Exec. Order No. 13563, Improving Regulation and Regulatory Review (2011), https://perma.cc/6PR7-XF4W.

6. *See id.*

7. OFFICE OF MGMT. & BUDGET, EXEC. OFFICE OF THE PRESIDENT, REPORT TO CONGRESS ON THE COSTS AND BENEFITS OF FEDERAL REGULATIONS, https://perma.cc/9AX6-5VPM (archived March 27, 2020).

8. *See generally* OFFICE OF THE U.S. TRADE REPRESENTATIVE, EXEC. OFFICE OF THE PRESIDENT, AGREEMENT BETWEEN THE UNITED STATES OF AMERICA, THE UNITED MEXICAN STATES, AND CANADA, art. 3.16 (Dec. 13, 2019), https://perma.cc/7BNR-KFYQ.

purpose of the standard is "to advance regulatory approaches and trade policies that are transparent, and based on science and on risk for products of agricultural biotechnology . . . ."[9] USMCA carries out the standard by requiring specific measures related to agricultural biotechnology, but also by requiring "Good Regulatory Practices" such as using "the best, reasonably obtainable information, including scientific, technical, economic, or other information . . . ."[10]

III. UNITED STATES REGULATION OF GENE EDITED AGRICULTURAL CROPS

The broadly accepted regulatory principles outlined by Presidential Administrations should underlie United States policies to enable use of gene editing for agricultural crops. Gene editing in this context results in plants with similar genetic changes to those that could be developed through traditional breeding.[11] Placing these genetic changes in context of the long history of traditional breeding to develop safe and nutritious crops helps to orient our regulatory baseline. Regulatory policies that would regulate gene edited plants differently than traditionally-bred counterparts would not be based on the best available scientific and technical information, commensurate with risk, accommodate the more than thirty years of regulation of genetic engineering, nor provide consistency.

A policy approach that views gene edited plants in relation to plants developed using traditional breeding also adheres to the goals of the White House Office of Science and Technology Policy's Coordinated Framework for the Regulation of Biotechnology.[12] This policy was first published in 1986 and updated in 1992 and 2017.[13] It provides the foundation for the Federal regulatory system for biotechnology products among the United States Department of Agriculture (USDA), the Environmental Protection Agency (EPA), and the Food and Drug Administration (FDA).[14] The Framework aims "to prevent unnecessary barriers to future innovation and competitiveness by improving the transparency, coordination, predictability, and efficiency of the regulation of biotechnology

9. *Id.* at 3.16(3).

10. OFFICE OF THE U.S. TRADE REPRESENTATIVE, EXEC. OFFICE OF THE PRESIDENT, AGREEMENT BETWEEN THE UNITED STATES OF AMERICA, THE UNITED MEXICAN STATES, AND CANADA, art. 28.5(1)(a) (Dec. 13, 2019), https://perma.cc/4TKC-R9NW.

11. Ashley P. Taylor, *Companies Using CRISPR to Improve Crops*, THE SCIENTIST (Jan. 31, 2019), https://perma.cc/DD2Y-NH4W.

12. *See* OFFICE OF SCI. AND TECH. POLICY, EXEC. OFFICE OF THE PRESIDENT, MODERNIZING THE REGULATORY SYSTEM FOR BIOTECHNOLOGY PRODUCTS: FINAL VERSION OF THE 2017 UPDATE, https://perma.cc/JLV5-T7HG (archived Mar. 27, 2020).

13. *Id.* at 1.

14. *Id.*

products while continuing to protect health and the environment."[15] Important and relevant to gene edited products, the Framework also identifies that "[i]t is the characteristics of the biotechnology product, the environment into which it will be introduced, and the application of the product that determine its risk (or lack thereof)."[16] Agencies should not only follow "a risk-based approach to regulation," but "the regulatory system should distinguish between those biotechnology products that require a certain level of Federal oversight and those that do not."[17]

Recently, the USDA finalized a revision to 7 C.F.R Part 340 aimed at modernizing and streamlining its regulations to ensure that they are up-to-date with the best available science and take full advantage of the Agency's over thirty years of experience regulating products of biotechnology.[18] In the words of the Agency in its Notice of Proposed Rulemaking, the proposed regulations are intended to "modernize the Department's biotechnology regulations with a balanced approach that continues to protect plant health while allowing agricultural innovation to thrive."[19] This is a positive signal that the implementation of the revised Part 340 will achieve this goal.

Under the USDA framework, gene edited plants would not be subject to the agency's regulations for the movement of genetically engineered organisms if: (1) The genetic modification is a change resulting from cellular repair of a targeted DNA break in the absence of an externally provided repair template; (2) the genetic modification is a targeted single base pair substitution; or (3) The genetic modification introduces a gene known to occur in the plant's gene pool, or makes changes in a targeted sequence to correspond to a known allele of such a gene or to a.[20] The agency determined these categories of plants could otherwise be produced by traditional breeding methods. These traditional techniques, in the words of the Agency, "generally involve deliberate selection of those plants with desirable traits either from existing population genetic variations or from new genetic variations created through artificial hybridization

15. *Id.* at 6.

16. *Id.* at 7.

17. *Id.* at 8.

18. 7 C.F.R. § 340 (2020); Movement of Certain Genetically Engineered Organisms, 85 Fed. Reg. 29790, 29832 (June 6, 2019) (codified at 7 C.F.R. pt. 330, 340, 372), https://perma.cc/6X58-P4NX; Rick Coker & Lyndsay Cole, *USDA Proposes New SECURE Biotechnology Regulations to Protect Plant Health and Promote Agricultural Innovation*, USDA (June 6, 2019), https://perma.cc/AQ64-3L3N.

19. *Id.*

20. 7 C.F.R. § 340; Movement of Certain Genetically Engineered Organisms, 85 Fed. Reg. at 29832.

or induced mutations, and have been used since the advent of sedentary agriculture."[21] These proposed exemptions are appropriate notwithstanding that they do not fully reflect the diversity of genetic variability that can occur in nature or through traditional breeding techniques.[22]

Consistent regulation of traditionally bred plants and plants developed using gene editing techniques also appropriately extends the product- and risk-based foundation of the Coordinated Framework to gene edited plants. As the Agency notes, National Academies of Science (NAS) reports have long recognized and reaffirmed that there is no evidence of unique hazards inherent in the use of recombinant DNA techniques and, with respect to plants, crops modified by molecular and cellular methods should pose risks no different from those modified by classical genetic methods for similar traits.[23] Moreover, this consistent product- and risk-based treatment is more generally supported by the 2017 NAS report titled *Preparing for Future Products of Biotechnology*.[24] This report concludes by highlighting the importance of prioritizing "familiarity with a product, the complexity of the risk assessment for the product, and the anticipated risk associated with the product (that is, proportionate oversight) . . . ."[25]

Accordingly, the USDA correctly concluded "it is logical and appropriate to exempt from [Part 340] regulation plants produced by any method if they also could have been produced by traditional breeding."[26] It is clear that familiarity and proportionality are well-supported underlying tenets to be applied in the design and implementation of the regulatory framework for gene edited plant products.

21. *Id.* at 26519.

22. *See* Letter from Bruce Houtman, Leader of North America Regulatory Affairs, Corteva Agriscience, to Dr. Alan Pearson, Assistant Deputy Administrator, Biotechnology Regulatory Services (Aug. 6, 2019), https://perma.cc/HM44-MTTB.

23. *See* NAT'L RESEARCH COUNCIL, INTRODUCTION OF RECOMBINANT DNA-ENGINEERED ORGANISMS INTO THE ENVIRONMENT: KEY ISSUES 6 (1987) ("There is no evidence that unique hazards exist either in the use of R-DNA techniques or in the transfer of genes between unrelated organisms." "The risks associated with the introduction of R-DNA engineered organisms are the same in kind as those associated with the introduction into the environment of unmodified organisms and organisms modified by other genetic techniques."); NAT'L RESEARCH COUNCIL, FIELD TESTING GENETICALLY MODIFIED ORGANISMS: FRAMEWORK FOR DECISIONS 140 (1989); GENETICALLY ENGINEERED CROPS, *supra* note 3, at 31.

24. *See* NAT'L ACAD. OF SCI., PREPARING FOR FUTURE PRODUCTS OF BIOTECHNOLOGY (2017).

25. *Id.* at 164.

26. Movement of Certain Genetically Engineered Organisms, 84 Fed. Reg. 26514, 26519 (June 6, 2019) (codified at 7 C.F.R. pt. 340, 372).

As the EPA and FDA consider promulgating specific regulatory policies addressing gene edited plants, these policies must likewise be based on consistent product- and science-based regulatory foundations. In fact, each agency has an existing foundation on which to base gene editing regulatory policies.[27]

Under FDA's 1992 Statement of Policy for Foods Derived from New Plant Varieties, "The regulatory status of a food, irrespective of the method by which it is developed, is dependent upon objective characteristics of the food and the intended use of the food (or its components)."[28] Moreover, while "[t]he method by which food is produced or developed may in some cases help to understand the safety or nutritional characteristics of the finished food[,] . . . the key factors in reviewing safety concerns should be the characteristics of the food product, rather than the fact that the new methods are used."[29] This formulation of policy can apply to foods from new plant varieties developed using gene editing, or any other breeding method, including biotechnology.[30] By using our accumulated knowledge of plant genomes and biotechnology over the last thirty plus years, FDA's current policy approach for food developed from new plant varieties can efficiently and consistently address food developed from gene edited plants.

In EPA's 2001 publication of its current rule addressing the registration requirements for "plant-incorporated protectants," EPA's regulatory trigger for plants that have been genetically engineered to express a pesticidal substance—they recognized "plant breeding in the United States has a good record of providing a safe food supply and that plant breeders employ accepted standards of practice to maintain this record."[31] There is a long history of safety associated with the types of changes that could be accomplished using transitional breeding techniques or found in nature and the self-regulating aspects of plant breeding (e.g., field testing and breeder observations).[32] This history supported EPA's determination that it could effectively exempt such plants from pre-market regulatory oversight.[33] The EPA should explicitly extend this rationale to any plant-incorporated protectant produced from a gene edited plant—maintaining a consistent, proportionate, and science-based policy for plants that, other than the process used in their development, are otherwise indistinguishable.

27. *See generally* OFFICE OF SCI. AND TECH. POLICY, *supra* note 12.

28. FDA, STATEMENT OF POLICY - FOODS DERIVED FROM NEW PLANT VARIETIES (1992), https://perma.cc/9JHW-BQ6L.

29. *Id.*

30. *Id.*

31. Plant-Incorporated Protectants, 66 Fed. Reg. 37772, 37783 (July 19, 2001) (codified at 40 C.F.R. pt. 152, 174).

32. *See id.*

33. *See id.*

Collectively, the USDA, FDA, and EPA have the opportunity to set the foundation for a coordinated regulatory policy for gene edited plants that adheres to the principles of the Coordinated Framework and longstanding United States regulatory principles. As repeatedly noted, to do otherwise risks hindering access to important products, stigmatizing innovation, and decreasing our ability to adapt to future agricultural challenges.[34]

IV. CORTEVA'S GENE EDITED WAXY CORN

Corteva's innovative next-generation waxy corn developed using CRISPR-Cas9 gene editing is a specific example of a plant variety with a familiar food safety profile,[35] and thus regulatory policies should it treat no differently than a traditionally bred plant product. Traditionally bred waxy corn varieties have been grown in the United States since the 1940s for their differing starch composition.[36] With gene editing, higher yielding next generation waxy corn products can be developed more efficiently, which increases productivity and our ability to quickly develop locally adapted products.

The waxy corn characteristic is determined by a mutation in the corn's waxy gene, Wx1.[37] There are over 200 known spontaneous or induced mutations in the maize Wx1 gene that result in gene disruption and the waxy characteristic.[38] These mutations consist of insertions or deletions of various sizes; from several base pairs to the entire gene.[39] Just as with traditionally bred commercial waxy corn, gene edited waxy corn developed using CRISPR-Cas9 has a mutation in the Wx1 gene, loss of Wx1 gene function, and the intended waxy characteristic.[40] In this way, next generation waxy corn is indistinguishable from a variety that could arise in nature or otherwise be developed with traditional breeding methods.

As the USDA confirmed consistently with the foregoing discussion of its regulatory policy, it had no reason to believe gene edited waxy corn would be a

34. *See* STEVE OLSON & MARIA DAHLBERG, TRENDS IN THE INNOVATION ECOSYSTEM 34 (2013) ("Overly cautious or burdensome regulations can be another reason why innovations originating in the United States are commercialized elsewhere.").

35. Taylor, *supra* note 11.

36. DEBORAH SCHWARTZ & ROY WHISTLER, HISTORY AND FUTURE OF STARCH 5 (2009).

37. NINA DUENSING ET AL., NOVEL FEATURES AND CONSIDERATIONS FOR ERA AND REGULATION OF CROPS PRODUCED BY GENOME EDITING 6 (Jeorg Romeis ed., 2018), https://perma.cc/35MA-24KU.

38. *Id.*

39. *Id.*

40. *Id.*

plant pest under the Plant Protection Act.[41] Thus, the USDA considers gene edited waxy corn to be regulated just as a traditionally bred product would be (e.g., subject to any applicable "Plant Protection and Quarantine (PPQ), permit and/or quarantine requirements.").[42]

V. CONCLUSION

We face a future where innovation-driven solutions will be imperative to meet the challenge of sustainably producing healthy and nutritious food. Gene editing has tremendous potential to be used to increase sustainability and resilience in our food system. It does this by building on the same plant breeding principles farmers and plant scientists have used for thousands of years: planting seeds, observing characteristics, and advancing the most desirable selections—albeit in a more precise and efficient manner.

Our regulatory policies for gene edited plants should rely on the best available scientific and technical information, efficient while commensurate with risk, and accommodate new evidence and learning. Further, it should be consistently applied and enforced to foster innovative products of gene editing for the benefit of farmers, consumers, and the environment.

Regulatory policies should recognize gene edited products—indistinguishable from those that could be found in nature or developed using traditional breeding—should be regulated in the same manner and be based on the characteristics of the end-product.

We must not, however, succumb to believing the only way a regulatory system protects human health and the environment is to outlaw innovation or make a regulatory system so burdensome and onerous that it functionally prevents adoption. Regulatory policies that encourage and foster innovation will be required to better adapt to changing climates, to reduce our environmental impact, to increase resistance to crop devastating diseases, and to ensure our food system's ability to sustain into the future.

41. Letter from Michael J. Firko, Ph.D, APHIS Deputy Administrator, USDA, to Dr. Daria H. Schmidt, North America Director of Registration and Regulatory Affairs, DuPont Pioneer (Apr. 18, 2016), https://perma.cc/6WRQ-5LM8.

42. *Id.*